BRAIN.

PART IV., 1898.

Original Articles and Clinical Cases.

PATHOLOGY OF A CASE OF FRIEDREICH'S DISEASE.

With a Summary of previously reported cases.

BY H. MACKAY, M.D.

THE case of Friedreich's disease, the morbid anatomy of which I here report, was one of a family described clinically in the *American Journal of the Medical Sciences*, vol. cviii., 1894, p. 151.

To save the trouble of reference, I append here a brief note of the clinical condition of the patient during life.

H. W., male, unmarried, aged 26 at the time of examination, was one of a family, three members of which, *i.e.*, two sisters and himself, have been under my observation for Friedreich's disease. A fourth member, a sister, had already died from the same complaint. There is no hereditary transmission of the disease, but various spinal neuroses are present in collateral relatives of the patient, and a second cousin probably died of the same disease.

The patient suffered from measles and scarlet fever in his sixth year, soon after which weakness of the legs and staggering appeared. At twelve he was unable to move about; at fourteen the arms began to be attacked, and by his twenty-second year these limbs were helpless.

He came under my notice about this time and presented a typical picture of the later stage of the disease. His power of voluntary movement was limited to slight motion at the joints of the upper limbs, raising and rotation of the head, and some control over the muscles of expression. He was also able to roll

over in bed, and to raise the trunk on the elbows when supine. His deep and superficial reflexes were abolished, with the exception of normal pupillary reactions to light and accommodation. His sensation was everywhere well preserved, and his special senses acute.

Coördination had been much impaired before the limbs became fixed. He had lateral nystagmus and frequent twitchings in the facial muscles. His speech was laboured and explosive. His intelligence was good, and he had complete control over bladder and bowel. The spine showed a lateral curvature. The optic discs were normal.

The patient suffered from asthma, and from cardiac enfeeblement, but without recognisable dilatation or valvular disease.

In the winter of 1897, when 30 years of age, he contracted measles for the second time. Symptoms of collapse speedily supervened, with cyanosis and heart failure from which he died.

The autopsy, some twenty-eight hours after death, showed the following. Permission to open the chest was not obtained.

Cranium.—Much adhesion of Pacchionian bodies, otherwise no abnormality.

Membranes.—Normal; no excess of fluid in subdural space.

Brain.—To naked-eye inspection normal. The grey and white matter were natural on section, and the convolutions well marked.

Cerebellum.—Well developed and of average size. Measurements in the three chief planes:—11·8 c.m. × 5·3 c.m. × (between vermiform processes) 4 c.m. Schultze gives, as average figures, 11·5 c.m. to 12·5 c.m. × 5·25 c.m. to 7·5 c.m. × 3 c.m. to 4 c.m.

Medulla.—Visibly smaller than normal. Vagi, hypoglossi, and other cranial nerves appear to be normal.

Cord.—The dural sac is loose and baggy, and the contained fluid excessive in amount. The latter looks like normal cerebro-spinal fluid. The dura appears thickened, but the pia has no abnormal appearance. The cord is evidently shrunken in size. On section the posterior column is everywhere greyish and translucent, and the same appearance is visible in the posterior part of the lateral columns. The posterior spinal roots are visibly shrunken in size. The anterior appear normal.

The contents of the cranium, and the spinal cord, were placed in Müller's fluid, together with portions of the following peripheral nerves: the sciatic and the anterior crural of the right side, the anterior tibial and internal plantar of the left side. From the upper limbs were taken portions of the right

median and ulnar, and of the left radial and posterior interosseous. These latter were hardened in Erlitzky's fluid followed by methylated spirit.

For defining the areas of degeneration in the cord and medulla, preference was given to Schäfer's modification of the Pal-Weigert method. By this process, myelin-bearing fibres, whether healthy or degenerating, stand out in black or blue-black against the white ground of sclerosed or non-medullated tissue. For differentiating healthy from degenerate myelin, Hamilton's modification of Marchi's process was used. For investigating the neuroglia, to which, since the appearance of Déjérine and Letulle's observations [8] considerable interest has attached, attempts were made to use Weigert's—now classical —1895 method,[33] but owing to the hardening of the material in Müller's fluid, the attempt was not successful. Mallory's 1895 method [34] failed also for the same reason. Better results were obtained by a preliminary stain in Van Gieson's fluid, followed by Mallory's phospho-molybdic or phospho-tungstic hæmatoxylin.[35] By this means an excellent triple stain is obtained, in which the dark axis-cylinders and glia cells are well distinguished from medullary sheaths (yellow) and connective tissue other than glial (red-violet). For the peripheral nerves Schäfer's method answered admirably, while for axis-cylinders aniline blue-black, benzopurpurin, or Mallory's hæmatoxylin was used. For the spinal ganglia toluidin-blue and eosin, hæmatoxylin and eosin, or picro-carmine were employed.

The actual changes found were as follows :—

Cord.

T. S. Lower Lumbar (L. V. and IV.)

Posterior Column.—There is well marked sclerosis, most marked in the posterior part of the column. At the level of the 5th lumbar this involves the posterior third of the column. The anterior third, next to the commissure, shows a large number of well-preserved fibres, but also a few swollen and degenerate ones. The middle third of the column shows a gradual transition between the conditions described. In the posterior third very few stained fibres can be seen, and these are scattered at wide intervals throughout the sclerosed area. A band of comparatively well-preserved fibres lies along the mesial side of the posterior horn on each side, separating the sclerosed portion from the grey matter. This, which is continuous with the well-pre-

served fibres lying dorsal to the commissure, evidently represents Marie's cornu-commissural tract.

Of the posterior root fibres, those entering the gelatinous substance (middle group of Lenhossek), those entering Burdach's column (mesial group), and those occupying Lissauer's border-zone are all intensely degenerated, the course of individual fibres passing horizontally being marked generally by isolated droplets of myelin, while those transversely divided display swollen sheaths and an absence of axis-cylinders.

The sclerosed area includes the septo-marginal tract of Bruce and Muir and the central oval tract of Flechsig, neither of which contain healthy fibres.

At the level of L. IV. the dark stained fibres occupy only the anterior fourth of the posterior column. The remaining three-fourths are degenerated, the posterior portion the most severely. About the centre of the posterior column, however, a small, linear tract of fairly well-preserved fibres appears, bordering the posterior fissure. This has not the oval shape of Flechsig's *centrum ovale*, and probably corresponds to a portion of Bruce's septo-marginal tract.

Lateral Column.—At the lower level, L. V., there is apparent under the low power a lightening of the myelin stain in a triangular area occupying the posterior part of the column, but separated from the posterior horn by the well-preserved fibres of the lateral limiting layer. At the higher level, L. IV., the degeneration is more pronounced, and corresponds with the position of the crossed pyramidal tract. In connection with Marie's view[86] that the degenerated area in the lateral column does not represent the crossed pyramidal tract, it was noted that the degeneration affected equally the large and the small fibres of the area. It is equally true, however, that many large fibres remained unaffected throughout the tract. As will be seen afterwards, the size of the lateral sclerosed area diminished from the mid-dorsal region upwards, but it increased from the lumbar to the mid-dorsal region, and at the latter level well-marked degeneration appeared in the fibres of the direct pyramidal tract, which might account for the lateral diminution from that level upwards. There is distinct neuroglial overgrowth present, with an increase in the number of round, granular glial nuclei.

Anterior Column.—Normal.

Grey Matter. Posterior Horn.—There is extensive degeneration both of the vertical (ascending) and of the transverse (entering) fibres in the caput cornu.

FIG. 1.

FIG. 2.

There is no trace of any healthy nerve cells, while the adjoining large cells of the intermediate grey substance are well preserved. The reticulum of fine medullate fibres in the substance of the horn is fairly but not well, preserved.

Anterior Horn.—The large motor cells with their processes, and the fibrillar plexus are well preserved.

The Central Canal is occluded by a mass of small, round cells, which take on nuclear stains deeply. No trace of ependymal epithelium remains.

The posterior roots, spinal ganglia, and anterior roots will be described in detail later. It is sufficient here to say that the posterior roots were intensely sclerosed.

Upper Lumbar and Lowest Dorsal L. I. to D. XII.

Posterior Column.—At this level the postero-median fissure is for the first time recognisable. Previously—at lower levels—it had only been obscurely suggested, and had contained no prolongation from the pia. There is as yet no differentiation of Goll's from Burdach's column.

The area of stained medullate tissue in the P.C. is now limited to the tract of cornu-commissural fibres, which fill the apex of the posterior column, and occupy its lateral margins close to the grey matter. This area, however, contains a considerable number of swollen and otherwise degenerate fibres.

Lateral Column.—The degeneration of the C.P. tract is now well marked. It occupies a triangle, whose posterior base, separated from the posterior cornu by the thick layer of the lateral limiting zone, extends inwards from the periphery for about half the length of the posterior cornu. The apex reaches anteriorly to the level of the posterior commissure.

Anterior Column.—Normal.

Posterior Horn.—At the base of the posterior horn two or three shrunken cells can with difficulty be made out. There is a thin plexus of fine myelinised fibres anterior to the substantia spongiosa. The trabeculæ of the latter are thickened and numerous large Deiter's cells are visible. The vertical fibres, as well as the entering root fibres are degenerated.

Anterior Horn.—Apparently normal.

Clarke's Column.—This appears on each side as a faintly indicated white disc. Its posterior half is sclerosed. At its anterior pole, on each side, a thin plexus of fine fibres is visible, together with a few shrunken cells.

Lower Dorsal.—D. X.

Posterior Column.—There is still no trace of the differentiation of Goll's from Burdach's column. The whole breadth of the posterior column is occupied by the greyish white area of sclerosis. Some dark stained medullate fibres still occupy the apex and lateral boundaries of the column—in the site previously occupied by the cornu-commissural tract (ascending fibres from posterior roots?)—but these show an increasing number of degenerating fibres.

Lateral Column.—The patch of lateral sclerosis now takes on an extension forwards along the periphery of the column, the increase probably corresponding to the area of the direct cerebellar tract. This marginal degeneration reaches forward to a level corresponding to one-third of the peripheral circuit from posterior root to anterior fissure. The anterior portion of the degenerate tract is much less affected than the posterior.

Anterior Column.—There is now some disappearance of nerve tubes, with swelling and disintegration of others, and increase of interstitial tissue, in the anterior tips of Turck's columns on each side, where these border on the anterior fissure.

Posterior Horn.—The condition is the same as that described in the lumbar region.

Anterior Horn.—There is apparently some diminution in the number and volume of the internal group of motor cells.

Clarke's Column is completely sclerosed, both as to cells and fibres.

Mid-Dorsal. D. VII. to D. IV.

Posterior Column.—The narrow strip of medullated tissue bounding the commissure and posterior cornua shows a progressive loss of healthy fibres.

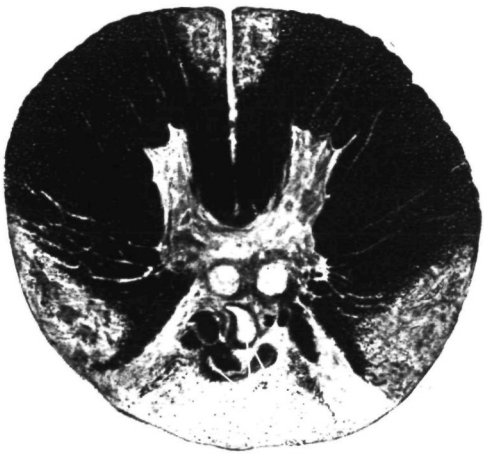
Lateral Column.—The degeneration in this column reaches its maximum extent about D. V. and at that level occupies a triangle, elongated anteriorly—whose base covers rather more than half the width of the lateral column, while the apex reaches the level of the summits of the anterior cornua. The lateral limiting layer is still preserved.

Anterior Column.—The sclerosis of the tips of Turck's column is well marked.

Posterior Horn.—This seems to be shrunken in size—the caput cornu reaching less than half way to the periphery. Its condition is as already described.

Anterior Horn.—No fresh changes are visible.

Clarke's Column.—Sclerosed.



a *b*

FIG. 3.

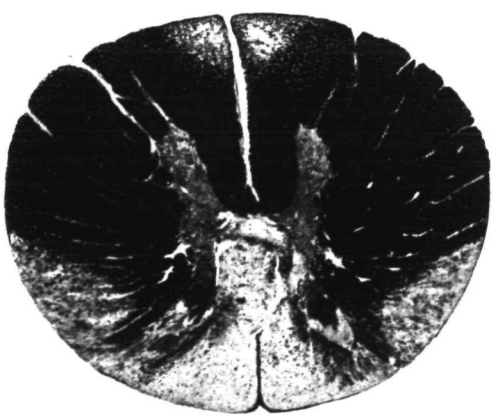


FIG. 4.

From D. VI. to D. III. an abnormality was present in the posterior column. A rounded patch of dense, sclerosed tissue occupied the anterior angle of the column, close to the commissure, displacing the fibres previously present there. These latter were represented in all probability in a ring-like whorl of medullated and partially degenerate fibres, which occupied the middle third of the column, posterior to the sclerosed patch already described. The whorl of fibres enclosed a second circular sclerosed area, and the remainder of the posterior column was occupied by sclerotic tissue as at former levels.

Upper Dorsal. D. II. to D. I.

The sclerosis of the *posterior column* here reaches its maximum, the remnant of stained fibres in the lateral tracts of Burdach's column, and posterior to the commissure, having undergone still further diminution.

Lateral Column.—The anterior marginal extremity of the sclerosed area does not extend so far forward as previously, having reached its maximum extent at the mid-dorsal region.

Anterior Column.—There is well-marked and symmetrical sclerosis of the anterior third of Turck's column. Degenerate tubes and increased neuroglia can be made out in the remainder of the direct pyramidal tracts on each side.

The shape of the cord departs from the normal here, being more oval than is usual at this level. This may possibly be due to antero-posterior shortening, caused by sclerotic changes in the anterior and posterior columns.

At the upper dorsal region, viz., D. I., there is apparent for the first time a distinct differentiation of Goll's from Burdach's column. A further change that takes place from this level onwards is the appearance of an increasing number of healthy, medullated fibres in the postero-external fields of Burdach's columns.

Lower Cervical. C. VIII. and VII.

Posterior Column.—The increase in the healthy fibres in Burdach's column now extends over the whole of that tract, and serves to distinguish it from Goll's tract. The increase in healthy fibres is also apparent in Lissauer's tract, which, though still much degenerated, yet contains more black-stained fibres than previously. Goll's column remains sclerosed up to the posterior commissure, and is shrunken to a narrow streak on each side the posterior fissure.

Lateral Column.—The position and degree of the sclerosis are as before. The anterior point reached by the degeneration in the D. C. T. is nearly on a level with the anterior commissure. In the upper sections of this region, however, there seems to be an increase in the thickness of the neuroglial trabeculæ in the position of Gower's tract, but without any distinct degeneration of the tubes.

Anterior Column.—There is well-marked and symmetrical sclerosis of Turck's column, appearing as a bluntly wedge-shaped tract on each side of the anterior fissure. The rest of the ground fibres are normal.

Posterior Horn.—This is distinctly atrophied and shrunken. There are a few nerve-cells in each cornu, but they appear below the normal size. The gleia cells are numerous and deeply stained. The preserved fibres with well-marked axis-cylinders, however, appear to be more numerous than previously.

Anterior Horn.—The inner or mesial group of cells has undergone diminution in number, and in size of the individual cells. The remaining groups, however, contain well-developed cells and processes.

Middle of Cervical Swelling. C. VI. to V.

An abnormality is again present in the posterior part of the cord at this level.

It commences at the level of C. VII. as a circumscribed oval-shaped area of sclerosed tissue, which occupies a position between the neck of the left posterior cornu and the adjoining portion of Burdach's column. The sclerotic area increases in size with successive sections, and reaches its maximum at the level of C. VI. In the position it occupies it displaces inwards towards the mesial line the streak of medullated fibres which has been described as bordering the internal margin of the posterior cornu. Its outer side is in contact with the lateral reticular formation. Completely sclerosed at its first appearance, at higher levels its area is traversed by scattered medullated fibres, a few of which are healthy but the greater number degenerated. By the level of C. IV. all traces of the abnormality have disappeared.

Posterior Column.—The condition is similar to that described previously. Burdach's column continues to receive an increasing number of healthy fibres, and also some degenerate ones. The healthy fibres are aggregated for the most part in the postero-external fields of the tract, adjacent to the posterior roots, and in Lissauer's tract. Goll's column also contains more myelinised

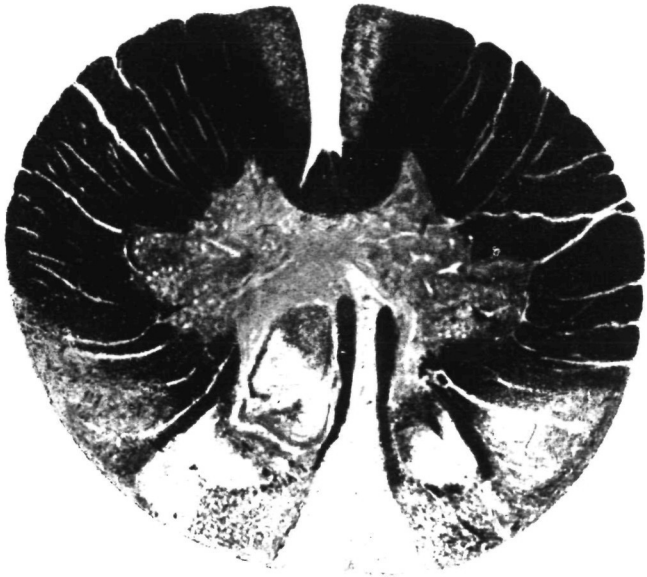


FIG. 5.

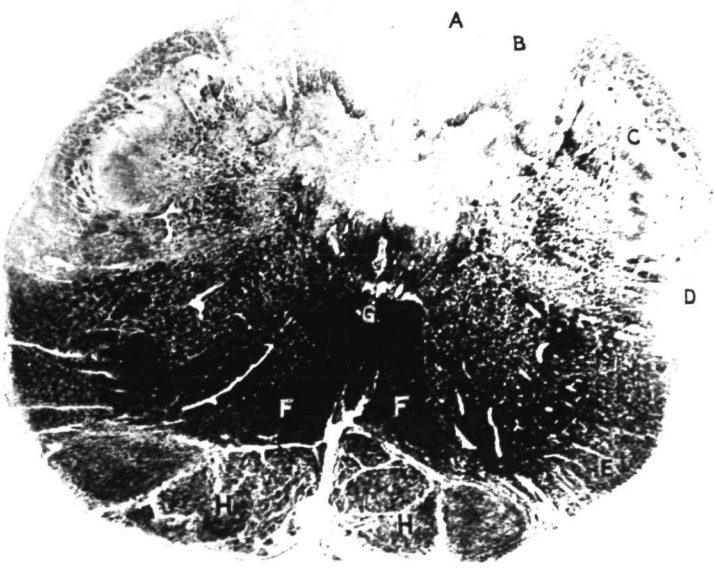


FIG. 6.

fibres than at former levels. These pass obliquely through the column towards the commissure, and many of them are degenerated.

Lateral Column.—The sclerosed area maintains its former position. The anterior extremity reaches further forward on the left side than on the right.

Anterior Column.—As before. The direct pyramidal tract on each side is symmetrically sclerosed. There is probably some increase of the neuroglia in the anterior ground fibres.

Posterior Cornua.—The abnormality on the left side has been already described. On the right side there is some improvement in the fulness of the fibrillar reticulum anterior to the substantia spongiosa.

Anterior Cornua.—There is asymmetry of the anterior horns, the right being larger than the left.

Upper Cervical. C. IV. to III.

Posterior Column. — Goll's tract is sclerosed throughout. Several fibres in advanced degeneration pass through it antero-posteriorly. These are more numerous near the commissure. Burdach's column, in its postero-external triangle, and Lissauer's tract contain a fair number of myelinised tubes, some of which contain healthy axis-cylinders.

Lateral Column.—The degenerate area is smaller in size than previously. The complete degeneration is limited to a small, oval area, which does not now reach to the periphery, and whose anterior limit does not pass beyond the level of the posterior commissure. The fibres of the D. C. tract, however, still contain many degenerated tubes.

Anterior Column.—Turck's columns still sclerosed.

Posterior Cornua.—Still degenerated and shrunken. The abnormality on the left side has now disappeared. Perhaps the fibrillar plexus is more stained than previously.

Anterior Cornua.—The right is still larger than the left. Both contain some shrunken cells in their anterior portions. The lateral groups of cells on each side are large and well developed.

Resumé of Cord-Changes.

Complete Sclerosis of Goll's Column from the sacral to the upper cervical region, most pronounced in the upper dorsal region.

Sclerosis of Burdach's Column (only recognisable as such above the level of the upper dorsal), the degeneration being constant in the portions adjoining Goll's column, and being less marked below in the parts bounding the commissure and the posterior cornua, and above in the postero-external fields.

Sclerosis of Lissauer's Tract less marked in the cervical region.

Sclerosis of the C. P. Tract, from lumbar region upwards, reaching its maximum at mid-dorsal level, and thereafter diminishing.

Sclerosis of D. P. Fibres, from mid-dorsal region upwards, increasing from below upwards.

Sclerosis of D. C. Tract, from lower dorsal region upwards. Most marked below.

Sclerosis of Posterior Horns and Posterior Roots throughout. Anterior horns well preserved, with the exception of a few cells of the mesial group and anterior group. Almost total escape of the anterior roots (to be described later).

Complete Sclerosis of Clarke's Column.

The condition of the nerve roots requires separate mention.

(A.) *Posterior Roots and Ganglia.*

These were examined: (*a*) above the ganglia; (*b*) in the ganglia; (*c*) below the ganglia; (*d*) in the mixed trunks.

The specimens were taken from the lumbar and dorsal region. I regret that the cervical roots were not preserved, all the more because the condition of the intra-medullary root-fibres in that region suggests that they would have shown, perhaps, a state of better preservation than those of the lower level. Cross-sections of the extra-medullary roots, however, were frequently included in sections of the cord in the cervical region, and an examination of these showed no marked difference between these roots in cross section and those belonging to other levels of the cord.

(*a*) The posterior roots between the ganglia and the cord showed extreme degeneration. Both by Marchi's and by Schäfer's method, only a very few dark-stained tubes of normal calibre were present in each root. In the unstained spaces between these larger fibres were seen fine small nerve-fibres, empty sheaths and connective tissue. The fine nerve fibres, probably the "embryonal" fibres of Auscher and Déjérine,[10] were frequently closely packed, in bundles of from six to twenty fibres, the individual

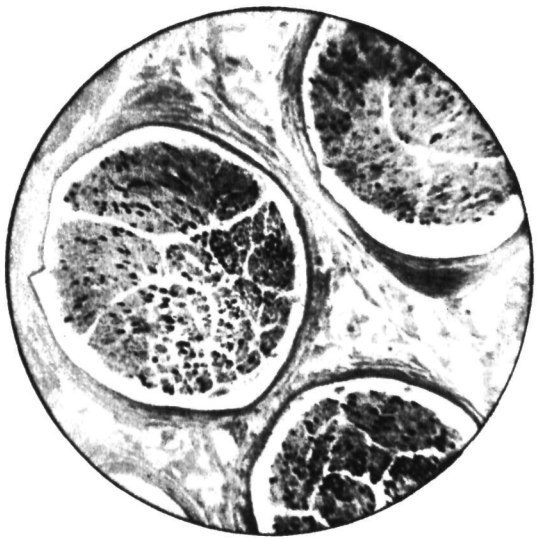


FIG. 7.

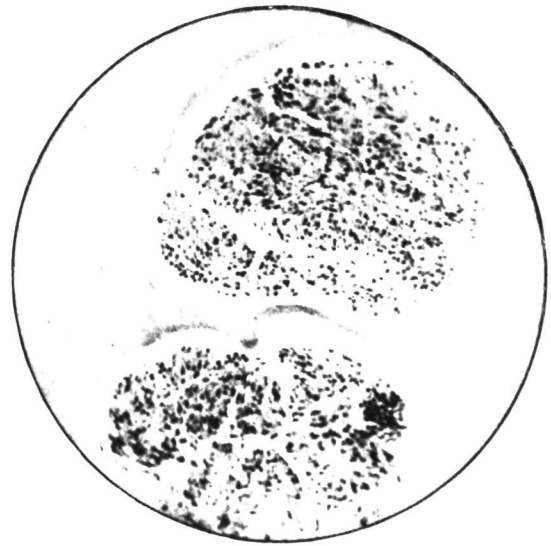


FIG. 8.

tubes measuring from 3 to 8 in diameter. Extremely fine, but well-stained axis-cylinders were present in most of them, and generally a very thin myelin sheath, but the latter remained unaffected by myelin stains such as Schäfer's and Pal-Weigert's. In others, the myelin seemed disintegrated and granular, and the axis-cylinders were sometimes hypertrophied, sometimes absent. The empty nerve-sheaths, both of the large and of the fine fibres, were recognised as rings, either round or distorted by pressure, their outlines being frequently marked in Marchi and osmium preparations by a marginal ring of fine black granules.

(*b*) In the spinal ganglia both ganglion cells and nerve fibres call for notice.

The cells, as indeed the ganglia themselves, appeared smaller than normal. Measurements through their longest diameters (when not perfectly round) gave their average diameters as 50μ, the limits between which they varied being from 25μ to 70μ. This is below the figure given by Lenhossék[28] for the average diameter of healthy cells of the larger sort, viz., 60 to 80μ. Striking was the amount of pigmentation they displayed. In very few was this limited to a mass lying between the nucleus and the thickened peripheral layer of cell plasma, or to a crescentic ring investing the nucleus. On the contrary, in the majority of the cells it occupied approximately two-thirds of the area of the cell plasma, obscuring the nucleus completely. It consisted of coarse pigment granules, insusceptible to stain, and agglomerated in many cases into dense clumps in which no differentiation of separate granules could be made out.

The cell plasma was invariably opaque and turbid, never in the least degree brightly refractile or translucent. It stained readily with plasma stain and then showed itself finely granular in structure. The finer details of the granules could not be made out owing to shortcomings in the staining, due to my want of familiarity with Mann's method. No vacuolation was present, but the normal marginal space between cell plasma and capsule figured and described by Lenhossék was frequently present. The nuclei were occasionally well defined as also were the nucleoli, but not in every cell. The cell processes also could only seldom be distinguished. The epithelium of the capsules appeared normal.

I am unable to venture on an opinion as to how far these appearances are abnormal or the expression of artefacts. The latter explanation readily suggests itself in connection with the shrinking in size. But, on the other hand, the method of harden-

ing used by Lenhossék, from whom the normal measurements are taken, viz., corrosive sublimate and alcohol, would cause as much shrinking as the Müller's fluid and alcohol used in my own preparation. The amount of pigmentation that may be considered normal is another vexed question. Wollenberg, who discusses the matter,[22] apparently concludes, with Obersteiner, that the decision as to what is and what is not pathological is frequently an arbitrary one. The opacity of the cell plasma may —according to Trzebinski (quoted by Wollenberg, *loc. cit.*)—be produced by the Müller's fluid and alcohol employed. I can speak definitely only as regards vacuolation and fatty degeneration of the plasma, neither of which could be recognised in these sections.

On the whole, a comparison with the few normal specimens I possess leads me to the opinion that the ganglion cells were smaller and more pigmented than average normal cells. Whether this, however, corresponds with the pigmentary atrophy described by other observers, I am unable to say.

In the fasciculi of transversely divided nerve-fibres which appeared in the sections of the ganglia, it was easy to recognise marked degeneration. Numerous lacunæ were present, corresponding to spaces vacated by swollen medullary sheaths that had disappeared in handling. Many of the fibres showed granular and disintegrated myelin, and from many the axis cylinders had disappeared. Between these were spaces occupied by connective tissue, fine fibres, some apparently healthy, some undergoing degeneration, and empty Schwann's sheaths.

Logwood preparations showed a distinct multiplication of connective tissue nuclei, both in the endoneurium between the nerve fibres and in the interstitial tissue between the ganglion cells.

(*c*) *Below the Ganglia.*—The roots showed the same condition of degeneration as already described.

(*d*) *The Mixed Trunks.*—Tranverse sections here showed the two roots lying within a connective tissue-sheath apparently much too large for its contents.

The constituent portions of the nerve were easily recognised, in Pal-Weigert and Schäfer preparations, the anterior root showing, for the most part, regular and well stained fibres of uniform size, while the posterior showed a few dark stained discs and rings in the midst of a mass of unstained sclerotic tissue.

The Anterior Roots.—These consisted, for the most part, of large nerve tubes, of 10-12μ in diameter, with healthy sheaths and axis cylinders. They were not wholly free, however, from degenerative change. This affected chiefly the myelin sheath.

In some the myelin had separated from the Schwann's membrane and appeared loose in the interior of the tube. In others it was aggregated into a mass lying against the inner wall of the sheath. In others, again, the myelin appeared to have become absorbed, leaving a naked axis cylinder inside the tube so formed. This condition, well shown in benzo-purpurin and Mallory-hæmatoxylin preparations, appeared to resemble the denudation of the axis cylinder described by Babinsky and others as occurring in multiple sclerosis. A few fine fibres in good preservation were present in the anterior roots, but in much smaller numbers than in the posterior.

The Peripheral Nerves.

Those examined were the sciatic in the upper part of the thigh, the anterior crural, anterior tibial, internal plantar, median, ulnar, radial and posterior interosseous. Each and all of these showed extreme degeneration. By Schäfer's method not only the healthy medullated sheaths, but those also which contained degenerate but unabsorbed myelin, gave the black reaction. The unstained areas, therefore, corresponded to parts which were totally devoid of myelin, either healthy or degenerate.

To obtain a comparative estimate of the degrees of this degeneration various methods were adopted.

A modification of Sakaky's method[25] was used for estimating the number of healthy fibres in the fasciculi. By means of a mm. stage micrometer and a corresponding ruled ocular the number of healthy fibres present in a series of squares each with a side measurement of ·1 mm. was counted, and an average was taken from nine or sixteen of these squares. Observations on healthy nerve fibres gave 32 nerve fibres of 10 to 12μ each in diameter as the average normal contents of such a square. With the normal figure of 32 was compared the number of healthy fibres per ·1 mm. square in the best preserved portion of the cross section of the nerve. The small fibres, of which large numbers were apparent in all of the peripheral nerves, were excluded from the calculation on account of the difficulty of getting any satisfactory estimate of their number in normal nerves.

As regards the larger fibres, it was found that in the majority of the nerves examined, viz., in the median, radial, posterior interosseous, sciatic, anterior crural, and internal plantar, occasional fields could still be found in which a few squares reached or approximated to the normal content of fibres.

In the ulnar and anterior tibial, however, in not a single field

in the cross section of the nerve could an area containing 32 healthy fibres per square ·1 mm. be found.

The relative degree of sclerosis was roughly estimated by measuring the largest superficial areas in each nerve in which not a single healthy medullated fibre could be found.

The results may be thus tabulated:—

In *the posterior interosseous nerve* a whole field measuring ·3 mm. in diameter	contained not a single healthy fibre.
In the ulnar, a space measuring ·3 × ·15 mm.	" " " " "
In the radial, a space measuring ·2 × ·2 mm.	" " " " "
In the median, a space measuring ·18 × ·18 mm.	" " " " "
In the anterior tibial, a space measuring ·175 × ·175 mm.	" " " " "
In the internal plantar, a space measuring ·125 × ·15 mm.	" " " " "

In the sciatic and anterior crural nerves no sclerotic area larger than ·1 mm. square void of healthy fibres could be found.

Contrary to one's expectation, it thus appeared that the greatest destruction of nerve fibres had taken place in the mixed nerves of the upper limb. In the nerves of the lower limb it appeared that portions more peripherally placed suffered greater degeneration than those nearer the cord. Connective tissue hyperplasia was extreme in those fibres in which the sclerosis was most marked, and reached its maximum in the internal plantar. In the same nerve the accompanying artery showed an extreme thickening of the intima, the lumen of the vessel being almost obliterated thereby. In the sciatic and anterior crural there was a great deposit of fat in the interfasicular connective tissue.

The degeneration in every case was of the ordinary parenchymatous type, the medullary sheaths being either granular, broken into clumps, disintegrated, with formation of droplets, or absorbed. Persistence of the axis-cylinders, such as was observed in the anterior roots, was nowhere seen in the peripheral nerves.

The Medulla.

Sections were cut from the whole length of the medulla with the exception of the region of the pyramidal crossing, which was unfortunately destroyed in removing the parts. The changes met with may be sufficiently described at three levels.

(*a*) Between the pyramidal decussation and the lower level of the olives.

The longitudinal fibres at this level comprise the funiculi graciles and cuneati, the lateral and pyramidal columns, and the two narrow layers which, lying on each side of the middle line dorsal to the anterior pyramids, represent the fibres of the inter-olivary layer or fillet.

It is these latter fibres and the adjoining tracts of the antero-lateral ground fibres which, alone of the longitudinal bundles, present healthy fields of well-stained fibres at this level. Of the remainder, the funiculus gracilis (Goll's column) maintains its former condition of almost complete sclerosis. The funiculus cuneatus (Burdach's column), better preserved than the preceding, shows a slender band of stained fibres along the margin which adjoins the central grey matter. In the lateral columns there is a general lightening of the stain, amounting in the region of the D. C. tract to complete sclerosis. Gower's tract shows here more definite signs of degeneration than were apparent in the cord. In the pyramids, there is a general faintness of the medullary stain, and, as was to be expected from the condition of the direct and crossed pyramidal tracts, numerous degenerated fibres are present.

Of the grey matter, the clavate nucleus is practically absent, being represented only by a very few rounded nerve cells.

The cuneate nucleus is also poorly developed, being considerably below its normal bulk. The caput cornu posterioris, however, now swelling into the tubercle of Rolando, appears to be recovering from its former atrophy, and shows a well-developed head of grey matter and numerous small, nucleated cells. The central canal appears normal. The ependymal lining is distinctly columnar, and outside the epithelial layer is a loosely-arranged gleial network, with numerous Deiter's cells.

The healthy and well-developed condition of the fillet layers already referred to occasioned some surprise, on account of the meagre development of the innermost strands of the internal arcuate fibres. These latter, proceeding from the nuclei of the posterior columns, bend round the central grey substance, and after decussating give rise to the fibres of the fillet layers. Owing probably to the sclerosis present in the clavate nucleus and the poor development of the cuneate nucleus, the strands passing from these nuclei to the fillet decussation are less full and less numerous than in a normal medulla. Some bundles of well-stained arcuate fibres which are present arise from the neighbourhood of the posterior horn, and occupy the outermost division of the internal arcuate fibres.

(*b*) Lower level of the inferior olive.

The healthy fibres of the fillet layers now appear as the well-stained interolivary layer, and, dorsally to these, the median area of the reticular formation is occupied by well-stained fibres, which, according to Ferrier,[45] are contributed from the anterior root-zone of the cord. The lateral area of the reticular formation is less well preserved. Towards the dorsal margin of the lateral column there is a considerable accession of healthy, dark-stained fibres apparent in cross section, and these are evidently related to the dark-stained bundles of internal arcuate fibres which are seen to proceed to the region of the corpora restiformia from the olives and the fillet.

The clavate nucleus is still absent as such from the postero-internal column, but traces of grey matter with infrequent round cells can be made out in its site.

The caudate nucleus is now well developed, and contains numerous nerve cells.

The olivary bodies are well developed, and the numerous fibres passing from them show the black stain of normal myelin.

The central grey matter and the posterior longitudinal fasiculus also appear normal.

The pyramids, however, are smaller than normal, and still contain many degenerated fibres.

(*c*) Upper level of olive (at and above calamus scriptorius).

The prominent feature from this level upwards is the gradual increase in the healthy fibres of the corpus restiforme of each side by the continued accession of arcuate fibres from the olivary bodies.

There still appears a small area of sclerosis in the site occupied by the direct cerebellar fibres. The pyramids continue of smaller bulk than normal, but they exhibit less evident signs of degeneration than at lower levels.

The cranial nuclei (XII. and X.) appear to be normal. The fibres of the fillet and of the posterior longitudinal fasiculus are well stained and healthy.

From this level upwards the medulla and pons exhibit no marked morbid change.

Cerebellum.

No signs of degeneration or maldevelopment could be found in the cerebellum. The inferior peduncle showed healthy fibres and axis-cylinders throughout. The plicæ showed a normal

arrangement, with a well-marked nuclear layer, and numerous healthy Purkinje's cells.

Remarks on the Case.

In its clinical features and its post-mortem appearances, the case reported shows no peculiarity. With the former I do not intend to deal, as the matter has been so recently and exhaustively treated by Mackie Whyte in this Journal.[42]

None of the pathological conditions described are new to the literature of the disease, with the trivial exception, perhaps, of the abnormal arrangements described as occurring in the posterior column of the cord, in the upper dorsal and mid-cervical regions.

In many features the case bears a close resemblance to some of the more recently reported cases, *e.g.*, those of Simon (16, in summary of autopsies), Bonnus (*ib.* 17), Mirto (*ib.* 13), and Guizetti (*ib.* 12). In four of these, viz., 12, 16, 17, and my own, the degeneration of the posterior column reached its maximum in the dorsal region. In the same four cases the cornu-commissural tract, and fibres representing Flechsig's oval tract, escaped injury either relatively or entirely.

The degeneration of the crossed pyramidal and direct cerebellar tracts, recorded in nearly every reported case, was present in these cases too. In addition Lissauer's tract was more or less affected in each, as it was also in cases 11 and 10.

In all, as indeed in every recorded case where they have been examined, the posterior roots were sclerosed. The condition of the spinal ganglia is not mentioned in cases 16 and 17. In 12 and 13, however, as also in Blocq and Marinesco's case, 11, and probably also in my own, 18, changes were present. Interstitial hyperplasia, with changes in the ganglion cells, vacuolation, or shrinking, are mentioned in every case.

In the medulla, sclerosis of the posterior columns, with degeneration of nuclei, is recorded in cases 12, 16, 17, 18, and also in 11, and degeneration, in the bulb, of the direct cerebellar fibres, is also recorded in cases 11, 12, 16 and 18.

Similar changes in the posterior columns of the medulla are reported by Friedreich (cases 2 and 4), and were also observed in the doubtful cases of Brousse and Tedeschi.

Some degeneration of the fibres of the anterior pyramids occurred in Guizetti's case and my own.

The cerebellum has been found normal in every case in which its condition has been recorded, with the exception of Auscher's doubtful case.

The peripheral nerves were atrophied or degenerated in cases 12, 13, 17 and 18, severely so in the last case.

In the light of these cases, together with the fact that similar changes have been recorded by Friedreich and by Rutimeyer, it must be admitted that degeneration of the peripheral nerves, which may reach an extreme degree, ought in future to find mention in any complete account of the morbid anatomy of Friedreich's disease.

The nature of the fine fibres observed in the peripheral nerves in this as in other cases of Friedreich's disease is a question of great interest.

Auscher[10] describes those present in his case as fibres having embryonal characters, *i.e.*, with an axis-cylinder, and either a very slight myelin sheath or none at all. He expressly states that he found no degenerated tubes nor empty sheaths.

Guizetti[11] records the presence of numerous fine fibres with a diminution in the number of coarse fibres. He describes and figures various histological conditions of the fine fibres in the nerves and the posterior roots, viz., some—a majority—with axis cylinders, some without, some apparently deprived of medullary sheaths, and others in which the sheaths stained slightly with osmic acid. He assumes these conditions to be the result of atrophy.

In my own case several varieties of fine fibres could be distinguished, viz. :—

(*a*) Fine fibres with a slender axis-cylinder and an apparently medullated sheath. I say *apparently* because the substance of the sheath, though colouring with plasma stains, and very faintly also with chromatin stains, yet

failed to take up the specific myelin stains, such as those of Weigert and Schäfer. This fact has been noted also by Tedeschi.[15]

(*b*) Fine fibres showing more or less traces of degeneration, *e.g.*, (*a*) a granular condition of the sheath, (*β*) hypertrophy of the axis cylinder, either with or without a thin investment of myelin, or (*γ*) disappearance of the axis cylinder.

(*c*) Empty fibres, myelin and axis-cylinder having undergone absorption, the Schwann's sheaths remaining having frequently fine granules, staining black with osmium, attached to their inner surfaces.

All these appearances have been noted and described in the degeneration of peripheral nerves which accompanies various scleroses of the cord. Westphal figures them in a case of postero-lateral sclerosis (*Archiv. für Psychiat.*, Bd. viii., taf. xi.), and again in a case of central and peripheral degeneration due, he thinks, to tubercular infection (*ib.*, Bd. xvi., taf. xi.). Sakaky,[26] and Oppenheim and Siemerling,[28] describe them in the peripheral neuritis accompanying cases of tabes. Many observers have described the arrangements of the fine fibres as being in closely packed clusters or fasciculi, as if held together by some outer investment. Oppenheim and Siemerling (*loc. cit.*) describe bundles of well-preserved rods of fine calibre inside the empty Schwann's sheaths of larger fibres. These observations suggest the presence of fibrils of regeneration rather than that of atrophied fibres.

Since Déjérine has shown[29] that the peripheral degeneration in some cases of tabes attacks first the distal extremity of the peripheral neuron, and may co-exist with complete integrity of the spinal ganglion and posterior spinal root, it is reasonable to suppose that the peripheral degeneration in cases of sclerosis of the cord, such as those alluded to above, may be akin to that which occurs in the toxæmic states due to lead, alcohol, diphtheria, &c. In these, as Gombault,[37] S. Mayer,[38] Pitres and Vaillard,[39] Gudden,[24] and others have described, there occurs, after the degenerative period, an outbudding of small regenerative fibres (" seg-

ments intercalaires," "schaltstucke"), which, in cross-section, would present the characters of the fine fibres described under (*a*). Indeed, it seems difficult to account in other ways for the presence of these fine medullated and cylindered fibres in the midst of otherwise general degeneration. If Fleming's view[31] be correct, that the normal fine fibres in peripheral nerves are the first to undergo degenerative changes, the fine fibres under discussion can hardly represent the original fine fibres present normally in every peripheral nerve, and unless simple atrophy of nerve fibres can take place without a trace of molecular change or disintegration, it is equally difficult to conceive these fine fibres as originating in the atrophy of the larger ones. It seems, at least, equally probable that they may be single or multiple regenerative fibres, the outcome of the segmental neuritis of larger tubes. Further, there is no cause hindering the degeneration in their turn of the fine regenerative fibres. As Gudden remarks[24] (p. 731):—"One factor only need be assumed, viz., that the patient is a debilitated individual, and that the toxic virus does not at once escape from the system. In such a case the restitution, in the first place, of the nerve fibres, proceeds slowly, and secondly, these latter, when scarcely in working order, either through the feebleness of the organism or through the presence of some fresh virus. . . . are checked in their further development and again fall into decay." Gudden instances as an illustration of "fresh virus" the infection of tubercle, and it is noteworthy that if the doubtful cases of Friedreich's disease in the appended list be included, a history of tubercle is present in seven out of the twenty-two autopsies recorded.

Such a process as is suggested above would well account for the appearances found in the fine fibres in classes (*b*) and (*c*). It may be objected to this explanation of the presence of the fine fibres that the primary pathological processes, central and peripheral, in Friedreich's disease, have not been shown to depend on any toxæmic dyscrasia, inherited or acquired. The same objection, however, applies equally to amyotrophic lateral sclerosis, and to the

hereditary form of muscular atrophy. These diseases affect the peripheral motor neurons, much, it appears to me, as Friedreich's disease affects the peripheral sensory neurons associated with muscle. In both these forms of muscular atrophy Gombault has observed [37] in the degenerate peripheral nerves the occurrence of segmental neuritis with regenerative processes.

The extreme preponderance of the degeneration in the posterior roots rather than the anterior indicates that it is the afferent fibres of the peripheral nerves that are chiefly attacked. The fact, moreover, frequently recorded, that the patients' sensibility to touch, pain, and temperature remains unimpaired throughout, suggests that it is the afferent nerves from muscles that chiefly suffer. This agrees with Guizetti's conclusion, who was of opinion that in his own case there existed a systematic atrophy of sensory fibres. In his case, however, he considered that muscular and cutaneous fibres were both affected, and it should be remembered that, clinically, the patient's tactile and thermic sensibility were diminished below the knees, and that some tactile impairment was present in the hands.

The presence of abnormal arrangements in the structure of the cord which I have described as occurring in the dorsal and cervical portions is suggestive of structural anomaly dating back to the developmental period of the cord. Sections containing these abnormalities were variously stained in the endeavour to ascertain the finer structure of the growths. The nerve fibres traversing the areas were invariably degenerated, and none of them possessed axis cylinders. The intervening ground substance resembled closely the sclerotic tissue present in the posterior parts of Goll's column, and its density opposed a serious obstacle to its examination. The felt-like tissue composing it shrank extremely in the process of dehydrating and clearing, so that thin sections were destroyed by the tearing consequent on the shrinkage. Deiter's cells, however, could not be distinctly recognised, but corpora amylacea were present in considerable numbers. The staining reactions were those of glial tissue, and in all probability the structure was that of

a circumscribed gliomatous mass of long standing, in which the cellular elements seemed to have disappeared.

Finally, no appearance at all corresponding to Déjérine's description of whorls of glial tissue could be recognised in this case. The grey sclerotic areas in the posterior and lateral columns were found histologically to have the usual structure of neuroglial hyperplasia elsewhere. Numerous large Deiter's cells were present, frequently of elongated or lanceolate shape, as if obliquely-lying elongated cells had been divided in a plane approximating that of their longest diameter. In all, or nearly all, the faintly stained granular nucleus could be recognised, and in some the processes could be traced for a short distance from the cell. These elongated cells and smaller rounded ones formed dark-stained masses in a dense spongy-looking groundwork, the minute dark points in which probably corresponded to gleial fibres in cross-section. The cells were least distinct, and stained less freely in the older and more completely sclerosed areas, while they stained most distinctly in the transition zones between healthy and degenerating tissue. Where they stained least distinctly, *e.g.*, in the peripheral portion of the posterior columns, there numerous corpora amylacea were thickly strewn, and the converse of this arrangement held equally true, viz., the corpora amylacea were least numerous in those regions where the glial cells were most distinct. The same histological features characterised the areas of degeneration in the various columns of the cord. No special peculiarities could be made out in the lateral areas of sclerosis. The vessels and capillaries were nowhere markedly thickened, but were everywhere distended with blood cells.

The last mentioned fact is of interest in relation to the vascular theory of the causation of the disease which was favoured by Pitt, and by Blocq and Marinesco. These observers found changes in the blood vessels of the posterior columns, as also did Schultze in his second case, and Everett Smith.

On the other hand such changes were absent in the cases of Rutimeyer, Déjérine and Letulle, Guizetti, and in my own.

Guizetti, who discusses this matter, points out that disease of the posterior vascular system of the cord would leave unexplained the condition of the posterior roots and spinal ganglia, and that Clarke's column, which is invariably sclerosed, is supplied by the anterior system of vessels. Moreover, that such vascular dilatations as Pitt and Blocq and Marinesco have recorded, are a frequent accompaniment of sclerosis of the cord, and probably secondary to it.

On the whole it appears that our present knowledge of the pathogenesis of the disease cannot be better summed up than in Guizetti's conclusion, that Friedreich's disease depends upon a congenital predisposition, in consequence of which, in the early years of life, certain systems of fibres and nerve cells undergo a process of progressive atrophy, and that the process is independent of any contributory effect from vascular alterations.

To Guizetti's conclusion might be added that by "certain systems of fibres and cells" ought perhaps to be understood the following :—

(*A*) (Due to arrested development at the eighth month?) Tracts in the cord which are the latest to undergo medullation, viz., the pyramidal tracts, direct and crossed, and the postero-internal tract.

(*B*) (Secondary to mal-development of Goll's column?) Systems of fibres and cells functionally related to the postero-internal tract. The extent of the atrophic process as to systems attacked, and degree of degeneration in individual systems, may be dependent upon the duration of the disease. These systems may include :—

(*a*) The peripheral sensory neuron complex in its entirety, viz., peripheral sensory fibres, ganglion cells, posterior roots and root-zones (Burdach's, Lissauer's), fibres to Clarke's columns, to the middle zone, and to the anterior cornua.

(*b*) Portions of the central sensory neurons, viz., cells in posterior horns, with associated ascending fibres, cells in Clarke's columns, with associated fibres (direct cerebellar tract), cells in middle zone, with associated fibres (Gower's tract), cells in medullary nuclei, clavate and cuneate, with associated fibres (internal arcuate).

The atrophic changes in every system are arrested in the medulla, when the level of the lower olive is reached.

I append a summary in tabular form of the pathological conditions present in the autopsies of Friedreich's disease to which I have been able to refer, and I believe the list is fairly complete up to the date of its compilation (July, 1898). A useful summary of most of the cases included was given by Tedeschi [15] in 1896. I have excluded from the list all cases of the cerebellar type of the disease with which Nonne, Menzel, Marie, Sanger Brown and others have made us familiar, because it is clear—*pace* Senator—that these form a group quite distinct, clinically as well as pathologically, from the type described by Friedreich.

I have also placed in a separate list the doubtful cases of Kahler and Pick, Brousse, Auscher, and Tedeschi.

Kahler and Pick's case presents some close resemblances to hereditary ataxia. The age at onset—on menstruation, at 16—the general course of symptoms, the loss of knee-jerk, the impaired speech, the preserved pupil reflex, and the ataxia, all agree with Friedreich's symptom-complex. In addition spinal curvature was present, and a sister of the patient is said to have been affected similarly to herself.

On the other hand, Westphal (*Archiv. für Psychiat.*, Bd. ix., p. 697), draws attention to the early onset of paralytic weakness in the case, with outstretched legs and pointed toes, as dissociating it from Friedreich's group. In addition, nystagmus was absent, and there is no mention of choreiform movements, or of pes cavus.

Very similar to Kahler and Pick's case is that of Erlicki and Rybalkin [40] affecting also a young girl soon after puberty. In this case the rude strength of the legs was well maintained during the early period, and the majority of the symptoms of Friedreich's disease were present. On the other hand, deformity of the feet and spine were absent, as also were nystagmus and speech affection. More important, perhaps, was the hurried course of the disease, the symptoms developing with undue rapidity, and death ensuing from tubercular diarrhœa in twenty months from the onset. For this reason I have omitted the case.

Brousse's and Auscher's cases both concern women of later age, 24 years and 24½ respectively. In the former neither spinal nor foot deformity was present, nor, apparently, nystagmus. In the latter the reflex to light was absent, and post-mortem, brain and cerebellum were found of small size, while the lateral columns of the cord were unaffected.

In Tedeschi's case, as Mackie Whyte has pointed out,[42] many important clinical details are unfortunately omitted, *e.g.*, the condition of the knee-jerks, state of the spine, &c. The onset of the symptoms was anomalous, the arms being attacked before the legs, the gait was tabetic in character rather than cerebellar, and the patient was insane.

A case reported by Mitchell Clarke[41] has also been omitted because the complication of cerebellar tumour which was present vitiates the pathological record for purposes of comparison.

It only remains for me to express my grateful acknowledgments to Sir T. Grainger Stewart, who suggested to me the examination of the peripheral nerves, and to Dr. Eurich of Bradford, for kind assistance in the technic of neuroglia staining.

SUMMARY OF AUTOPSIES ON UNDOUBTED CASES.

Case 1.

A.—*Name and Duration.*—Andreas Lotsch; 15 years ill. Died at 38; cause, typhoid.

B.—*Author and Reference.*—Friedreich. *Virchow's Archives*, Bd. xxvi., s. 391 and xxvii., s. 1, 1863.

C.—*Cord.*—Small.

D.—*Membranes.*—Dural sac contained fluid. Pia milky and thickened, soft adhesions to cord.

E.—*Posterior Column.*—Grey, translucent, firm, from above lumbar swelling to calamus. Sclerosis most marked above lumbar swelling. *Microscopically*—Atrophy of nerve tubes and presence in their place of a finely fibrillar connective tissue—made up, in part, of the shrunken Schwann's sheaths. Between these elements a finely granular ground substance, clearing with acetic acid, and then revealing many round and oval nuclei.

F.—*Lateral Column.*—Normal.

G.—*Anterior Column.*—Normal.

H.—*Posterior Horn.*—Normal.

J.—*Anterior Horn.*—Normal.

K.—*Clarke's Column.*—Normal.
L.—*Spinal Roots.*—Posterior roots atrophied.
M.—*Spinal Ganglia.*—No mention.
N.—*Peripheral Nerves.*—Some atrophy in sciatic. Less in nerves of cervical and brachial plexus. More intense degeneration in hypoglossi.
O.—*Central Canal.*—No mention.
P.—*Medulla.*—Corpora restiformia slightly attacked.
Q.—*Cerebellum.*—Normal.
R.—*Cerebrum.*—Normal.
S.—*Remarks.*—Walls of capillaries in affected areas show fatty globules.

Case 2.

A.—*Duration.*—Justinie Suss; 15 years ill. Died of typhoid at 31.
B.—*Author.*—Friedreich. *Virchow's Archives*, Bd. xxvi., s. 391 and xxvii. s. 1, 1863.
C.—*Cord.*—Small.
D.—*Memb.*—Pia thickened and adherent to dura and to cord.
E.—*P. Col.*—Sclerosed between lumbar and cervical swellings. Above the cervical swelling only a thin zone, next periphery affected. Postero-median fissure obliterated.
F.—*L. Col.*—Sclerosed between lumbar and cervical swellings in the parts adjacent to the posterior column, but to a less extent than the posterior column.
G.—*A. Col.*—Normal.
H.—*P. Horn.*
J.—*A. Horn.*
K.—*Clarke's Col.*
} Grey matter of cord sclerosed in dorsal region.
L.—*Sp. Roots.*—Posterior roots atrophied.
M.—*Sp. Ganglia.*
N.—*Peri. Nerves.*—Interstitial hyperplasia in the nerve trunks of the extremities.
O.—*C. Canal.*—Occluded with small cells.
P.—*Med.*—Sclerosed in posterior column.
Q.—*Cbl.*—Normal.
R.—*Cbr.*—Normal.
S.—*Remarks.*

Case 3.

A.—*Duration.*—Salome Suss; duration 14 years. Died at 28 of typhoid.
B.—*Author.*—Friedreich. *Virchow's Archives*, Bd. xxvi., s. 391 and xxvii., s. 1, 1863.
C.—*Cord.*—As in former cases.
D.—*Memb.*—Pia thickened and opaque, and adherent to dura.
E.—*P. Col.*—Sclerosed throughout, most marked in dorsal region.
F.—*L. Col.*—Sclerosed, in dorsal region, in posterior part of lateral column on left side.
G.—*A. Col.*
H.—*P. Horn.*
J.—*A. Horn.*
K.—*Clarke's Col.*

L.—*Sp. Roots.*—Posterior roots atrophied.
M.—*Sp. Ganglia.*
N.—*Peri. Nerves.*
O.—*C. Canal.*—A double canal containing fluid in cervical region.
P.—*Med.*
Q.—*Cbl.*
R.—*Cbr.*
S.—*Remarks.*

Case 4.

A.—*Duration.*—Fr. Suss; duration 27 years. Died at 42 of typhoid.
B.—*Author.*—Friedreich and Schultze. *Virchow's Archives*, Bd. lxx., s. 140.
C.—*Cord.*—As in former cases.
D.—*Memb.*—Pia thickened and opaque, and adherent to dura.
E.—*P. Col.*—Sclerosed throughout. In cervical region Goll's column chiefly attacked.
F.—*L. Col.*—Sclerosed, in posterior part, throughout whole length of cord. A small band of healthy tissue intervening between sclerosed tissue and posterior column.
G.—*A. Col.*—In the cervical region severe sclerosis of the right pyramidal tract, adjoining the anterior fissure. This extended upwards beyond the decussation, but did not extend downwards into dorsal region.
H.—*P. Horn.*—Atrophied.
J.—*A. Horn.*—Atrophy of grey substance at cervical swelling. Ganglion cells fewer and smaller than normal.
K.—*Clarke's Col.*—Cells atrophied.
L.—*Sp. Roots.*—Posterior roots atrophied.
M.—*Sp. Ganglia.*—Normal.
N.—*Peri. Nerves.*—Normal.
O.—*C. Canal.*
P.—*Med.*—Small. Sclerosed in Goll's and Burdach's columns, with atrophy of the ganglion cells of both nuclei. Anterior pyramids normal. Connective tissue hyperplasia, with corpora amylacea, in corpora restiformia as high as the level of cal. script.
Q.—*Cbl.*—Normal.
R.—*Cbr.*—Normal.
S.—*Remarks.*—Walls of vessels thickened, especially in neighbourhood of posterior column.

Case 5.

A.—*Duration.*—Charlotte Lotsch; duration 35 years.
B.—*Author.*—Schultze. *Virchow's Archives*, Bd. lxxix., s. 132.
C.—*Cord.*—Thin and flattened.
D.—*Memb.*—Pia thickened and opaque.
E.—*P. Col.*—Sclerosed. In the cervical region a strip of less degenerate substance, 1 mm. broad, remains, dorsal to the posterior commissure. Postero-external fields also contain some normal fibres.
F.—*L. Col.*—Posterior parts sclerosed up to the periphery, but the degeneration did not extend so far forward as in case 4.
G.—*A. Col.*—Both sides sclerosed for some distance from decussation downwards, in a comma-shaped tract.

H.—*P. Horn.*—No mention.
J.—*A. Horn.*—No mention.
K.—*Clarke's Col.*—Sclerosed.
L.—*Sp. Roots.*—Posterior sclerosed.
M.—*Sp. Ganglia.*—No abnormality.
N.—*Peri. Nerves.*
O.—*C. Canal.*
P.—*Med.*—Normal, except for some hypertrophy of connective tissue.
Q.—*Cbl.*
R.—*Cbr.*
S.—*Remarks.*

Case 6.

A.—*Duration.*—Clara S.
B.—*Author.*—Everett Smith. *Boston Medical and Surgical Journal*, October, 1885.
C.—*Cord.*—Asymmetrical, small.
D.—*Memb.*—Meninges injected and adherent to bone.
E.—*P. Col.*—Sclerosed; with exception of a small area lying dorsal to the posterior commissure.
F.—*L. Col.*—Sclerosis of crossed pyramidal tract.
G.—*A. Col.*—Sclerosis of direct pyramidal tract, bordering on anterior fissure, but less intense than in the posterior columns.
H.—*P. Horn.* } Nerve cells less numerous than normal, and much altered.
J.—*A. Horn.* }
K.—*Clarke's Col.*—No mention.
L.—*Sp. Roots.*—Posterior sclerosed.
M.—*Sp. Ganglia.*
N.—*Peri. Nerves.*
O.—*C. Canal.*
P.—*Med.*
Q.—*Cbl.*
R.—*Cbr.*
S.—*Remarks.*—Smith thinks the disease due to arrested development of some of the cells and fibres of the cord.

Case 7.

A.—*Duration.*—R. S.; duration 14 years. Died at 29 of cardiac dilatation and failure.
B.—*Author.*—Newton Pitt. *Guy's Hospital Reports*, 1887, p. 369.
C.—*Cord.*—Unusually small.
D.—*Memb.*—Unaffected.
E.—*P. Col.*—Sclerosed. Goll's column throughout. Burdach's column severely so in posterior part. Escape of a narrow strip bounding posterior horn and root, especially along anterior half.
F.—*L. Col.*—Sclerosis of crossed pyramidal and cerebellar tracts. Most marked in dorsal region; less so above. A strip of marginal sclerosis extends forward, anterior to the direct cerebellar tract (Gower's tract ?).
G.—*A. Col.*—Periphery slightly sclerosed above, extending, in lower cervical region, to antero-median fissure.
H.—*P. Horn.*—In some sections sclerosed.

J.—*A. Horn.*—Unaffected.

K.—*Clarke's Col.*—Sclerosed in some sections.

L.—*Sp. Roots.*—Posterior sclerosed; anterior normal.

M.—*Sp. Ganglia.*

N.—*Peri. Nerves.*—Radial and anterior crural showed no degeneration.

O.—*C. Canal.*—Double canal present at decussation of pyramids.

P.—*Med.*—Marked degeneration of funiculus gracilis; less severe of funiculus cuneatus. Some degeneration in funiculus rotundus.

Q.—*Cbl.*

R.—*Cbr.*

S.—*Remarks.*—Pitt associates the disease with a tendency to vascular degeneration and an ill-developed spinal cord.

Case 8.

A.—*Duration.*—H. Kern; duration 14 years. Died at 20.

B.—*Author.*—Rutimeyer. *Virchow's Archives*, Bd. cx., s. 215.

C.—*Cord.*—Small.

D.—*Memb.*—Pia thickened, numerous adhesions, and opaque.

E.—*P. Col.*—Sclerosed. Severe of Goll's column; less so of Burdach's. Escape of Lissauer's tract and of Flechsig's oval tract.

F.—*L. Col.*—Sclerosis of crossed pyramidal and direct cerebellar tracts, but less severe than that of posterior column. Escape of lateral limiting layer.

G.—*A. Col.*

H.—*P. Horn.*
J.—*A. Horn.* } Grey matter of cornua appears normal.

K.—*Clarke's Col.*—Sclerosed.

L.—*Sp. Roots.*—Posterior sclerosed, most markedly in dorsal region.

M.—*Sp. Ganglia.*

N.—*Peri. Nerves.*—Marked degeneration of sciatic and median.

O.—*C. Canal.*

P.—*Med.*—Small. Sclerosis of funiculi graciles and cuneati.

Q.—*Cbl.*

R.—*Cbr.*—Normal.

S.—*Remarks.*

Case 9.

A.—*Duration.*—B. Kern; duration 9 years.

B.—*Author.*—Rutimeyer. *Virchow's Archives*, Bd. cx., s. 215.

C.—*Cord.*—Small.

D.—*Memb.*—No sub-dural exudation; pia thickened.

E.—*P. Col.*—Sclerosed; with exception, in cervical and lumbar regions, of small fields, as in former case.

F.—*L. Col.*—Sclerosis of crossed pyramidal and direct cerebellar tracts, with escape of lateral limiting layer. Some marginal degeneration extends forward beyond region of D. C. T. (Gower's tract?) Lateral sclerosis most marked in the cervical region.

G.—*A. Col.*

H.—*P. Horn.*

J.—*A. Horn.*

K.—*Clarke's Col.*—Sclerosed.

L.—*Sp. Roots.*—Posterior sclerosed.
M.—*Sp. Ganglia.*
N.—*Peri. Nerves.*
O.—*C. Canal.*
P.—*Med.*—Small.
Q.—*Cbl.*
R.—*Cbr.*—Normal.
S.—*Remarks.*—Rutimeyer considered the degeneration in both these cases to be identical with that occurring in tabes.

Case 10.

A.—*Duration.*—Paul Par.; duration 11 years. Died at 21, of mitral stenosis and pulmonary apoplexy.
B.—*Author.*—Déjérine and Letulle. *La Médecine Moderne*, April, 1890.
C.—*Cord.*—Small.
D.—*Memb.*—Adherent.
E.—*P. Col.*—Sclerosed. Extreme sclerosis of Goll's column. Marked sclerosis of Burdach's. Sclerosis of Lissauer's tract.
F.—*L. Col.*—Slight sclerosis of crossed pyramidal tract. Medium atrophy of direct cerebellar tract.
G.—*A. Col.*—Unaffected.
H.—*P. Horn.*—Shrunken in lumbar region.
J.—*A. Horn.*
K.—*Clarke's Col.*—Atrophy of fibres and cells.
L.—*Sp. Roots.*—Atrophy of posterior roots.
M.—*Sp. Ganglia.*
N.—*Peri. Nerves.*
O.—*C. Canal.*—Peri-ependymal glioma.
P.—*Med.*
Q.—*Cbl.*
R.—*Cbr.*
S.—*Remarks.* — Déjérine described in this case whorls of neuroglial fibres, which in L. S. appeared as undulating intercrossing fibres of great length. While this was the condition of the sclerosed posterior columns, in the lateral column on the other hand the sclerosis was a vascular one, and was associated with thickening of the pial prolongations. The lateral sclerosis he considered secondary to a meningo-myelitis.

Case 11.

A.—*Duration.*—Suzanne Desch.; duration 9 years. Died at 19, of pulmonary phthisis.
B.—*Author.*—Blocq and Marinesco. *Archives de Neurologie*, May, 1890.
C.—*Cord.*—Small.
D.—*Memb.*—Normal.
E.—*P. Col.*—Sclerosed. Extreme sclerosis of Goll's column. Severe sclerosis of Burdach's column. Escape of Westphal's postero-marginal zone. Lissauer's tract affected below but intact above.
F.—*L. Col.*—Sclerosis of crossed pyramidal and of direct cerebellar tracts, most marked in dorsal region. In lateral column, dilatation of

vessels, with symmetrically placed hæmorrhagic exudates. Thickened pial trabeculæ are present in the sclerosed area. Gower's tract unattacked.

G.—*A. Col.*—Unaffected.

H.—*P. Horn.*—Diminution in number of large transversal fibres. Ascending fibres less affected.

J.—*A. Horn.*

K.—*Clarke's Col.*—Sclerosed.

L.—*Sp. Roots.*—Sclerosis of posterior roots. Most marked in lumbar region.

M.—*Sp. Ganglia.*—Attacked. Disappearance of fibres. Peripheral vacuolation of ganglion cells. Hypertrophy of connective tissue.

N.—*Peri. Nerves.*—Not examined.

O.—*C. Canal.*

P.—*Med.*—Loss of fibres from posterior pyramids, less marked in corpora restiformia. Anterior pyramids unaffected. Cerebellar tract degenerated. Above olive a cavity, apparently due to capillary dilatation. Destruction of fibres of raphe.

Q.—*Cbl.*—Normal.

R.—*Cbr.*—Normal.

S.—*Remarks.*—Blocq and Marinesco consider the lesions in all the columns affected to consist in atrophy of nerve fibres and thickening of neuroglia. The fibres present have no relation to the pial system. They consider the morbid change starts from blood vessels, but that there is also a developmental lesion.

Case 12.

A.—*Duration.*—A. G.; duration 18 years. Death at 28 from heart disease.

B.—*Author.*—Guizetti. *Riforma Medica*, June, 1893, and *Il Policlinico*, 1894, p. 438.

C.—*Cord.*—Small.

D.—*Memb.*

E.—*P. Col.*—Sclerosed; with exception of a tract posterior to commissure and adjacent to posterior cornua (cornu-commissural tract ?). Escape of Flechsig's "centrum ovale." Lissauer's tract degenerated in dorsal region. Degeneration less severe in cervical region, where there is improvement in Burdach's column.

F.—*L. Col.*—Many degenerated fibres in crossed pyramidal tract in lumbar and dorsal region. Fewer in cervical region. D. C. T., and Gower's tract attacked from dorsal region upwards. Escape of lateral limiting layer.

G.—*A. Col.*—Unaffected.

H.—*P. Horn.*—Atrophied, cells few and degenerated.

J.—*A. Horn.*—Normal.

K.—*Clarke's Col.*—Sclerosed.

L.—*Sp. Roots.*—Posterior roots sclerosed. Anterior healthy.

M.—*Sp. Ganglia.*—Diminution in size of ganglion cells with progressive atrophy of some. Compensatory hyperplasia of connective tissue.

N.—*Peri. Nerves.*—Much atrophied. Many fine fibres present.

O.—*C. Canal.*—Pervious for a short distance only.

P.—*Med.*—Degeneration of Goll's and Burdach's columns. Horizontal fibres unaffected. Some degenerated fibres in anterior pyramids.

Q.—*Cbl.*—Normal.

R.—*Cbr.*—Normal.

S.—*Remarks.*—Guizetti found no alteration of pial septa, or of blood vessels. The fine fibres in the peripheral nerves proceed solely from the posterior roots, and are therefore sensory. The fine fibres in the muscular branches have the same origin. Guizetti concluded that in this case of Friedreich's disease there existed a systematic atrophy of sensory nerves, both cutaneous and muscular.

Case 13.

A.—*Duration.*—L. P.; duration 5 years. Death at 19 from tubercular pleurisy.

B.—*Author.*—Mirto. *Giornale del'Assoc. dei Medici e Naturalisti*, Anno iv., 1893.

C.—*Cord.*

D.—*Memb.*

E.—*P. Col.*—Sclerosed. Goll's and Burdach's columns degenerated. Lissauer's tract attacked.

F.—*L. Col.*—Degeneration of crossed pyramidal tract, diminishing from below upwards. Slight degeneration of direct cerebellar tract, and of Gower's tract.

G.—*A. Col.*

H.—*P. Horn.* }
J.—*A. Horn.* } Thinning of nervous reticulum in anterior and posterior horns, with atrophy of cells. Most marked in dorsal region.

K.—*Clarke's Col.*—Extreme sclerosis.

L.—*Sp. Roots.*—Posteror roots sclerosed.

M.—*Sp. Ganglia.*—Atrophic degeneration of cells. Thinning of nervous reticulum. Hyperplasia of connective tissue.

N.—*Peri. Nerves.*—Motor nerves degenerated; sensory not examined.

O.—*C. Canal.*

P.—*Med.*

Q.—*Cbl.*—Normal.

R.—*Cbr.*—Normal.

S.—*Remarks.*—The sympathetic ganglia were also examined and found normal.

Case 14.

A.—*Duration.*—Female; duration 18 years. Died at 28 from diabetes and tuberculosis.

B.—*Author.*—Burr. *University Medical Magazine*, Philadelphia, June, 1894.

C.—*Cord.*

D.—*Memb.*

E.—*P. Col.*—Sclerosed. Extreme sclerosis of Goll's column; less severe of Burdach's; from lower lumbar to highest cervical region.

F.—*L. Col.*—Degeneration of C. P. T. from lumbar swelling to upper cervical region. Degeneration of D. C. T. from mid-dorsal to upper cervical.

G.—*A. Col.*—Degeneration of D. P. T. from mid-dorsal to upper cervical regions.

H.—*P. Horn.*—Slight affection of posterior horns. Degeneration of ganglion cells.

J.—*A. Horn.*—Atrophy of a few cells.

K.—*Clarke's Col.*—Marked degeneration.

L.—*Sp. Roots.*—Posterior sclerosed; anterior intact.

M.—*Sp. Ganglia.*

N.—*Peri. Nerves.*

O.—*C. Canal.*

P.—*Med.*

Q.—*Cbl.*

R.—*Cbr.*

S.—*Remarks.*—The reporter adheres to Dejerine and Letulle's theory of the nature of the changes in the posterior and lateral columns.

Case 15.

A.—*Duration.*—Male; duration 8 years. Died at 19.

B.—*Author.*—Dana. *Postgraduate*, New York, vol. xi., no. 7.

C.—*Cord.*—Small; flattened antero-posteriorly.

D.—*Memb.*—Pia thickened.

E.—*P. Col.*—Sclerosed most at lower levels.

F.—*L. Col.*—Sclerosed. Affecting C. P. T. and D. C. T., and to a more or less extent, Gower's tract. In addition, marginal sclerosis of nearly the whole circumference of the cord is present.

G.—*A. Col.*

H.—*P. Horn.*—Moderate degree of degeneration of grey matter affecting nerve cells.

J.—*A. Horn.*

K.—*Clarke's Col.*

L.—*Sp. Roots.*—Not examined.

M.—*Sp. Ganglia.*—Not examined.

N.—*Peri. Nerves.*—Not examined.

O.—*C. Canal.*

P.—*Med.*—Degeneration "probably" extended into medulla.

Q.—*Cbl.*

R.—*Cbr.*

S.—*Remarks.*—For clinical history see *Journal of Mental and Nervous Diseases*, vol. xv., 1890. Numerous holes (? perivascular spaces) ·5 to 2 mm. in size were scattered through grey and white matter of the cord. Presence of gliosis in sclerosed area could not be affirmed.

Case 16.

A.—*Duration.*—Ad. Rouzier; duration 5 years. Death at 17 from unexplained cause, not revealed on autopsy.

B.—*Author.*—Simon. *Le Progrès Médical*, September, 1897.

C.—*Cord.*—Small.

D.—*Memb.*—Thickening of soft membranes on posterior aspect of cord.

E.—*P. Col.*—Sclerosed. Most marked in dorsal region, but almost as

severely in cervical, too. Lissauer's tract attacked in sacral region, but cornu-commissural and septo-marginal fibres escape. In lumbar region, Flechsig's centrum ovale is attacked, but cornu-commissural fibres again escape.

F.—*L. Col.*—Sclerosed, but less so than posterior column. The C. P. T. and D. C. T. equally affected from the upper lumbar region upwards. The lateral limiting layer escapes.

G.—*A. Col.*—Direct pyramidal tract affected from upper dorsal region upwards.

H.—*P. Horn.*—Myelinic reticulum degenerated. Diminution in number and in volume of ganglion cells.

J.—*A. Horn.*—Diminution in number and volume of ganglion cells, but the motor cells of front part of the cornua are well developed.

K.—*Clarke's Col.*—Sclerosed.

L.—*Sp. Roots.*—Posterior roots sclerosed throughout; more so in lumbar and dorsal regions, less so in cervical.

M.—*Sp. Ganglia.*

N.—*Peri. Nerves.*

O.—*C. Canal.*

P.—*Med.*—Sclerosis of cuneate nucleus. More severe sclerosis of funiculus gracilis. Cerebellar bundle attacked.

Q.—*Cbl.*—Normal.

R.—*Cbr.*—Normal.

S.—*Remarks.*—The neuroglial tissue in the sclerosed areas is in some places arranged in perivascular whorls. Vessels but slightly altered. No marked proliferation of interstitial nuclei.

Case 17.

A.—*Duration.*—Jules G.; duration 13 years. Died at 39 of pleurisy (tubercular).

B.—*Author.*—Bonnus. *Nouvelle Iconographie de la Salpêtrière*, No. 3, 1898.

C.—*Cord.*—Small.

D.—*Memb.*—Healthy.

E.—*P. Col.*—Sclerosed. Most marked in dorsal region. Posterior and median radicular zones most attacked. Anterior radicular only affected above dorsal region. Lissauer's tract attacked in sacral and lumbar regions; less so in dorsal. Cornu-commissural tract and centrum ovale relatively, but not absolutely, preserved.

F.—*L. Col.*—Sclerosed, but less so than the posterior column. C. P. T. attacked throughout. D. C. T. attacked at and above dorsal region. Gower's tract also attacked.

G.—*A. Col.*—Direct pyramidal tract sclerosed in dorsal region, and still more affected in cervical region.

H.—*P. Horn.*

J.—*A. Horn.*

K.—*Clarke's Col.*—Sclerosed.

L.—*Sp. Roots.*—Posterior roots much degenerated.

M.—*Sp. Ganglia.*

N.—*Peri. Nerves.*—Median, sciatic, anterior tibial, and musculo-cutaneous degenerated.

O.—*C. Canal.*

P.—*Med.*—Goll's and Burdach's nuclei attacked; otherwise normal.

Q.—*Cbl.*—Normal.

R.—*Cbr.*—Normal.

S.—*Remarks.*—Bonnus's case was diagnosed as Friedreich's disease by Charcot. It was characterised by lightning pains, which have been recorded in Friedreich's disease by Charcot and Dejerine.

Case 18.

A.—*Duration.*—Henry W.; duration 24 years. Died at 30, of heart failure during measles.

B.—*Author.*—Mackay.

C.—*Cord.*—Small.

D.—*Memb.*—Healthy; some thickening of dura.

E.—*P. Col.*—Sclerosed. Maximum degree in upper dorsal. Least degree in lowest lumbar, where cornu-commissural tract escapes relatively. Some fibres of septo-marginal tract escape in mid-lumbar. Lissauer's tract sclerosed, but gradual improvement in same from upper dorsal region upwards. Posterior root zones improve *pari passu* with Lissauer's tract.

F.—*L. Col.*—Sclerosed. C. P. T. from lumbar enlargement to upper cervical. D. C. T. from lower dorsal to calamus scriptorius. Maximum degeneration in mid-dorsal region. Lateral limiting layer intact throughout. Gower's tract slightly attacked in cervical region.

G.—*A. Col.*—Direct pyramidal tracts on both sides sclerosed from lower dorsal upwards. Maximum in cervical region.

H.—*P. Horn.*—Sclerosed both in longitudinal and transverse fibres. Ganglion cells for most part absent. Fibrillar plexus poor in myelin.

J.—*A. Horn.*—Normal, except for some slight diminution in volume of motor cells.

K.—*Clarke's Col.*—Sclerosed.

L.—*Sp. Roots.*—Posterior sclerosed, but contain many fine fibres. Anterior show slight degenerative change.

M.—*Sp. Ganglia.*—Shrinkage and extreme pigmentation of ganglion cells. Increase of interstitial connective tissue. Degeneration of ascending fibres passing through ganglia.

N.—*Peri. Nerves.*—Sciatic, anterior crural, anterior tibial, internal plantar, median ulnar, radial and posterior interosseous, all extremely degenerated.

O.—*C. Canal.*—Occluded by round cells in most of its course. Normal above decussation of pyramids.

P.—*Med.*—Sclerosis of cerebellar tract. Sclerosis of funiculi graciles and cuneati. Some degeneration of pyramidal tracts and of Gower's tracts. Improvement of all parts after passing upper level of olives.

Q.—*Cbl.*—Normal.

R.—*Cbr.*—Normal.

S.—*Remarks.*—Vessels of cord healthy and distended with blood-cells, but no exudates. No perivascular whorls in glial tissue. Abnormalities, probably gliomatous, present in dorsal and cervical regions of cord.

SUMMARY OF AUTOPSIES ON DOUBTFUL CASES.

Case 1.

A.—*Duration.*—Strasik Josepha; duration 7 years. Death at 23. Mitral disease, and probably tuberculosis present.

B.—*Author.*—Kahler and Pick. *Archiv für Psychiatrie*, Bd. viii., s. 251.

C.—*Cord.*—Small.

D.—*Memb.*—Adhesion of dura and pia.

E.—*P. Col.*—Degenerated throughout, except a thin zone next grey matter.

F.—*L. Col.*—Posterior parts degenerated up to periphery. Lateral limiting layer unattacked. Crossed pyramidal tract more affected on right side than on left. Direct cerebellar tract degenerated.

G.—*A. Col.*—Right side degenerated down to dorsal region; left unaffected. (The reporters suppose there was an anomalous arrangement of decussating fibres).

H.—*P. Horn.* } No change in grey matter beyond a relatively feeble
J.—*A. Horn.* } development.

K.—*Clarke's Col.*—Sclerosed.

L.—*Sp. Roots.*—Anterior normal. Posterior sclerosed.

M.—*Sp. Ganglia.*

N.—*Peri. Nerves.*

O.—*C. Canal.*

P.—*Med.*—Normal.

Q.—*Cbl.*—Normal.

R.—*Cbr.*—Normal.

S.—*Remarks.*

Case 2.

A.—*Duration.*—Marie R.; duration 8 years. Died at 32 of phthisis.

B.—*Author.*—Brousse. *De l'ataxie héréditaire*, Paris, 1882.

C.—*Cord.*—No mention of size.

D.—*Memb.*

E.—*P. Col.*—Sclerosed. Most marked in lumbar region, and least in dorsal.

F.—*L. Col.*—Posterior parts sclerosed but not up to the periphery. Most marked in cervical and lumbar regions.

G.—*A. Col.*—Turck's column unaffected, but sclerosis present on both sides around heads of anterior cornua. Most extensive on left side.

H.—*P. Horn.*

J.—*A. Horn.*—Tips of cornua slightly affected in cervical region.

K.—*Clarke's Col.*—Not mentioned.

L.—*Sp. Roots.*—Not mentioned.

M.—*Sp. Ganglia.*

N.—*Peri. Nerves.*

O.—*C. Canal.*—"Inflamed." Lumen diminished by a collection of small embryonal cells. Complete obstruction in lumbar region.

P.—*Med.*—Slight sclerosis in posterior pyramids.

Q.—*Cbl.*—Normal.

R.—*Cbr.*—Normal.

S.—*Remarks.*—Apoplectiform attacks present in this case.

Case 3.

A.—*Duration.*—N. N., female; duration 4½ years. Died at 29 of pulmonary phthisis.

B.—*Author.*—Auscher. *Archives de Neurologie*, 1890, p. 475, and *Semaine Medicale*, July, 1890.

C.—*Cord.*—Small.

D.—*Memb.*—Normal.

E.—*P. Col.*—Sclerosed. (A neuroglial sclerosis with integrity of the vessels and pial prolongations.) Lissauer's zone intact.

F.—*L. Col.*—Unaffected.

G.—*A. Col.*—Unaffected.

H.— *P. Horn.*—Atrophied.

J.—*A. Horn.*

K.—*Clarke's Col.*—Atrophy of fibres and diminùtion of cells.

L.—*Sp. Roots.*—Posterior roots contain many "embryonal" fibres, but no empty sheaths.

M.—*Sp. Ganglia.*

N.—*Peri. Nerves.*—Sensory nerves show no degeneration of tubes or empty sheaths, but a great number of fibres with embryonal characters.

O.—*C. Canal.*—Replaced by a mass of epithelial cells.

P.—*Med.*

Q.—*Cbl.*—Small, but not degenerated.

R.—*Cbr.*—Small.

S.—*Remarks.*

Case 4.

A.—*Duration.*—Eg. Pall.; duration 6 years. Death at 18 from chronic pneumonia followed by marasmus.

B.—*Author.*—Tedeschi. *Beiträge zur Pathologischen Anat. und Allgemein. Pathol.*, Bd. xx., Hft. 1, 1896.

C.—*Cord.*—Small.

D.—*Memb.*—Dura normal. Pia thickened in posterior part.

E.—*P. Col.*—Sclerosed. Degeneration extending out to middle root zone. Escape of cornu commissural zone, and to a less extent of postero-internal root zone. Lissauer's tract attacked.

F.—*L. Col.*—Degenerated fibres in cervical region in area of D. C. T. At other levels merely abnormal thinness of nerve fibres.

G.—*A. Col.*—Abnormal thinness of nerve fibres.

H.—*P. Horn.* }
J.—*A. Horn.* } Thinning of nervous reticulum. Diminution and pigmentation of cells. Those of posterior horn shrunken and deformed.

K.—*Clarke's Col.*—Degeneration of cells. Thinning of fibrillar plexus.

L.—*Sp. Roots.*—Atrophied. The various fasiculi composed of extremely fine fibres which react very feebly with specific stains. Interstitial tissue increased.

M.—*Sp. Ganglia.*—Striking thinness of nerve fibres. Axis cylinders and myelin sheaths stain badly with their proper stains. Some cells vacuolated, some over-pigmented. Interstitial tissue increased.

N.—*Peri. Nerves.*—Not examined.

O.—*C. Canal.*—Double in lumbar region, becoming single at higher level.

P.—*Med.*—Sclerosis of Goll's and Burdach's funiculi. Longitudinal fibres diminished. Horizontal ones diminished and thinned. Cells less

numerous, shrunken, and pigmented. Reil's band appears unaltered both at origin and crossing. Pyramids, arciform fibres, and crura cerebri normal.

Q.—*Cbl.*—Normal size. Increase of pigment in Purkinje's cells. Thinning of fine plexus in nuclear layer.

R.—*Cbr.*—Normal.

S.—*Remarks.*—The patient was insane.

LITERATURE.

Autopsies on Friedreich's disease, including doubtful cases of the same.

[1] FRIEDREICH, *Virchow's Archiv*, Bd. xxvi., s. 329; *ib.*, Bd. xxvii., s. 1; *ib.*, Bd. lxx., s. 140.
[2] SCHULTZE, *Virchow's Archiv*, Bd. lxxix, s. 132.
[3] KAHLER AND PICK, *Archiv für Psychiatrie*, Bd. viii., s. 251.
[4] BROUSSE, *De l'ataxie héréditaire*, Paris, 1882.
[5] EVERETT SMITH, *Boston Medical and Surgical Journal*, 1885.
[6] NEWTON PITT, *Guy's Hospital Reports*, 1887, p. 369.
[7] RUTIMEYER, *Virchow's Archiv*, Bd. cx., s. 215.
[8] DEJERINE AND LETULLE, *La Médecine Moderne*, April, 1890.
[9] BLOCQ AND MARINESCO, *Archives de Neurologie*, May, 1890.
[10] AUSCHER, *La Semaine Médicale*, July, 1890, and *Archives de Neurologie*, 1890, p. 475.
[11] GUIZETTI, *Riforma Medica*, June, 1893, and *Il Policlinico*, 1894, pp. 438 and 453.
[12] MIETO, *Giorn. del' Assoc. dei Medici e Natural.* anno iv., 1893.
[13] BURR, *University Medical Magazine*, Philadelphia, June, 1894.
[14] DANA, *Postgraduate*, New York, July, 1896.
[15] TEDESCHI, *Beiträge zur Path. Anat. und Allgem. Path.*, Jena, Hft. 1, 1896.
[16] SIMON, *Le Progrès Médical*, September, 1897.
[17] BONNUS, *Nouvelle Iconographie de la Salpêtrière*, No. 3, 1898.

Autopsies on cases of the cerebellar type :—

[18] NONNE, *Archiv für Psychiatrie*, Bd. xxii., s. 273. (Case of the brothers Stüben. Cerebella small, but not atrophied. Purkinje's cells normal.)
[19] MENZEL, *Archiv für Psychiatrie*, Bd. xxii., s. 160. (Case of cerebellar atrophy, with cord changes similar to those of Friedreich's disease).
[20] FRASER, *Glasgow Medical Journal*, 1880. (Cerebellar atrophy, with normal condition of cord.)
[21] MEYER, BRAIN, part lxxix., vol. xx. (Autopsy on one of Sanger Brown's series. No circumscribed lesion in cerebellum. Degeneration of posterior columns, and of D. C. T. in cervical cord.)

The following have also been referred to :—

[22] WOLLENBERG, *Archiv für Psychiatrie*, Bd. xxiv., s. 213. (Changes in spinal ganglia in tabes. With plates and literature.)

[23] LENHOSSÉK, *Archiv für Psychiatrie*, Bd. xxix., s. 345. (Normal histology of spinal ganglion cells. With plates and literature.)
[24] GUDDEN, *Archiv für Psychiatrie*, Bd. xxviii., s. 643. (Changes in peripheral nerves in neuritis. With summary of literature on segmental neuritis and regeneration processes.)
[25] WESTPHAL, *Archiv für Psychiatrie*, Bd. viii., xiv., and xvi.
[26] SAKAKY, *Archiv für Psychiatrie*, Bd. xv., s. 584.
[27] NONNE, *Archiv für Psychiatrie*, Bd. xix., s. 352.
[28] OPPENHEIM AND SIEMERLING, *Archiv. für Psychiatrie*, Bd. xviii., s. 98.
[29] DEJERINE, *Archives de Physiol. norm. et path.*, 1884.
[30] DEJERINE, *Archives de Physiol. norm. et path.*, 1887. Also numerous papers in the same archives, vols. ii.-x., by HAYEM AND GILBERT, BABINSKI, PIERRET, PITRES AND VAILLARD, JOFFROY, VIGNAL and GOMBAULT.
[31] FLEMING, BRAIN, part lxxvii., vol. xx.
[32] WEIGERT, *Centralblatt für Allegemein. Path.*, Nov., 1890.
[33] WEIGERT, *Beiträge zur Kentniss der normalen menschlichen Neuroglia*, Frankfurt, 1895.
[34] MALLORY, *Centralblatt für Allgemein. Path.*, Oct., 1895.
[35] MALLORY AND WRIGHT, *Pathological Technique*, Philadelphia, 1898.
[36] MABIE, "Lectures on Diseases of Spinal Cord," Syd. Society's translation, 1895.
[37] GOMBAULT, *Comptes rendus de l'académie des sciences*, 1886, p. 489.
[38] S. MAYER, *Zeitschrift für Heilkunde*, bd. ii., 1886.
[39] PITRES AND VAILLARD, *Archives de Neurologie*, vol. xi., 1886.
[40] ERLICKI AND RYBALKIN, *Archiv für Psychiatrie*, Bd. xvii., p. 709.
[41] MITCHELL CLARKE, *Brit. Med. Journ.*, Dec. 8, 1894.
[42] MACKIE WHYTE, BRAIN, part lxxxi., 1898.
[43] FERRIER, "Functions of Brain," 1886.

DESCRIPTION OF PLATES.

(Staining in each case by Schäfer's method. Figs. 1-5 from microphotograph and sketch. Figs. 6 to 8 microphotograph only. Figs. 1-5, × 10 diameters. Fig. 6, × 8 diameters. Figs. 7 and 8, × 70).

FIG. 1.—T. S. at L. 4. Sclerosis of posterior column, except in anterior fourth. Also of posterior roots, root-zones, and cornua. Escape of fibres in position of Flechsig's *centrum ovale*. Slight degeneration of C. P. T. on each side.

FIG. 2.—T. S. at L. 1. Sclerosis of posterior columns, with exception of fibres in position of cornu-commissural tract. Also of posterior roots, root-zones, and cornua. Sclerosis of Clarke's Columns. Degeneration of C. P. T.

FIG. 3.—T. S. at D. 6. Structural abnormality in posterior column (developmental?).

(*a*) Semilunar area of sclerotic tissue, surrounded by a whorl of degenerate myelinised fibres.

(*b*) Capsule of sclerotic tissue enclosing a central medullated (degenerated) area, and in its turn enclosed by a layer of degenerated medullated fibres.

These latter probably represent those previously occupying the ventral fields of the posterior column, and bounding the posterior cornua.

FIG. 4.—T. S. at D. 2. Sclerosis of posterior column here reaches its maximum. Commencing improvement in root fibres, and in postero-external fields of Burdach's column. Atrophy of posterior cornua and Clarke's columns. Sclerosis of C. P. T., D. C. T. and D. P. T.

FIG. 5.—T. S. at C. 5. Abnormality in left posterior cornu. Structure somewhat similar to that described in fig. 3. Sclerosis of Goll's column. Improvement in postero-external fields of Burdach's columns. Well-stained fibres adjoining posterior cornua. Sclerosis of C. P. T., D. C. T. and D. P. T.

FIG. 6.—T. S. Medulla at decussation of fillet layers.

(*a*) Funiculus gracilis, and nucleus, sclerosed.

(*b*) Funiculus cuneatus, partially sclerosed, with poorly developed nucleus.

(*c*) Substantia gelatinosa. The fibrillar reticulum of the posterior cornu is fairly well myelinised.

(*d*) Direct cerebellar fibres, sclerosed.

(*e*) Gower's tract, slightly attacked.

(*f*) Fillet layers. Well-stained and healthy.

(*g*) Decussation of internal arcuate fibres. Their further course from posterior horn and Burdach's nucleus does not appear well in this section.

(*h*) Asymmetry and partial degeneration of anterior pyramids.

FIG. 7.—T. S. Sciatic. Schäfer. × 70.

FIG. 8.—T. S. Median. Schäfer. × 70.

By an oversight the following was omitted from the Description of the Cord in Mirto's case, No. 13 in Summary:—

Cord.—Small.

C. Canal.—Occluded.

Medulla.—Goll's and Burdach's columns degenerated as far as their nuclei. Integrity of cellular elements of nuclei. Band of Reil (*schleife*) healthy. Degeneration of D. C. T. could not be traced beyond pyramidal decussation. Pyramidal fibres normal at, and above decussation.